Complete Summary

GUIDELINE TITLE

External beam radiation therapy treatment planning for clinically localized prostate cancer.

BIBLIOGRAPHIC SOURCE(S)

Michalski JM, Roach M III, Merrick G, Anscher MS, Beyer DC, Lawton CA, Lee WR, Pollack A, Rosenthal SA, Vijayakumar S, Carroll PR, Expert Panel on Radiation Oncology-Prostate. External beam radiation therapy treatment planning for clinically localized prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 12 p. [111 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Roach M, Blasko JC, Perez CA, Beyer DC, Forman JD, Hussey DH, Lee WR, Paryani SB, Pollack A, Potters L, Scardino P, Schellhammer P, Leibel S. Treatment planning for clinically localized prostate cancer. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun;215(Suppl):1441-8.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Prostate cancer

GUIDELINE CATEGORY

Treatment

CLINICAL SPECIALTY

Internal Medicine
Oncology
Radiation Oncology
Radiology
Urology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of external beam radiation therapy for prostate cancer patients

TARGET POPULATION

Patients with clinically localized prostate cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Patient immobilization and positioning
2. Prostate localization using retrograde urethrography, computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound (US)
3. Radiation treatment planning
4. Radiation therapy

MAJOR OUTCOMES CONSIDERED

- Utility of radiologic imaging procedures in prostate localization
- 5-year biochemical disease free survival
- Toxicity and complications associated with radiation therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a

consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: External Beam Radiation Therapy Treatment Planning for Clinically Localized Prostate Cancer

Treatment	Appropriateness Rating	Comments
Simulation Imaging Tools		
CT	9	
Immobilization devices (external)	7	
Retrograde urethrogram (RUG)	6	
MRI (using endorectal	5	

Treatment	Appropriateness Rating	Comments
coil)		
MRI (using body coil)	5	
Immobilization devices (internal, rectal balloon)	4	
Bony anatomy 2D X-ray simulations	3	To verify isocenter only.
Treatment Planning		
IMRT	8	Most appropriate for patients treated with dose escalation.
3D-CT-based plan	7	
Proton beam RT	7	
2D-CT-based plan	2	
Non CT-based computerized plan	2	
Field Shaping		
IMRT	8	
3D BEV-designed blocks	7	
Manually designed blocks from x-ray simulation films or diagnostic CT scans	3	
No blocks	2	
Treatment Localization		
Daily localization with implanted fiducial markers (stereoscopic)	8	
Daily transabdominal ultrasound	7	
In room CT-based localization	7	
Daily port film or electronic image	6	

Treatment	Appropriateness Rating	Comments
localization: bony landmarks		
Weekly port films or electronic images	6	Will require larger PTV margins than daily localization.
Port film or image with initial treatment only	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Abbreviations

- BEV, beams-eye-view
- CT, computed tomography
- D, dimensional
- IMRT, intensity modulated radiation therapy
- MRI, magnetic resonance imaging
- PTV, planning target volume
- RT, radiation therapy

Summary of Literature Review

External beam radiation therapy for localized prostate cancer has evolved over the past two decades with the introduction of image-based treatment planning. External beam radiation therapy is a competitive alternative to radical prostatectomy and brachytherapy. When controlled for various case selection factors and quality of treatment delivery, outcome between the various modalities appears to be equivalent. Newer conformal radiation therapy methods, such as 3D conformal radiation therapy (3D CRT), intensity modulated radiation therapy (IMRT), and proton beam radiation therapy, have allowed radiation oncologists to improve the therapeutic ratio by lowering the dose to surrounding critical structures while simultaneously safely escalating the dose to the disease target. This review will detail the practical elements of radiation dose delivery, including patient set up and immobilization, target volume definition, treatment planning, treatment delivery methods, and tools to verify target localization during a course of external beam radiation therapy.

Patient Immobilization

The use of immobilization devices should allow the use of "tighter margins," reducing the dose received by surrounding normal tissues. Although some studies suggest that large day-to-day set up errors are significantly reduced with the use of patient immobilization devices, this conclusion is not universal. Some of the differences in conclusions reached by different studies may be explained by differences in the endpoints and methods of assessment. For example, in the one prospective series reporting no advantage to using immobilization, the percentage

of large errors (>5 mm) was not selectively evaluated. Furthermore, based on the findings of this study it is clear that immobilization devices that obscure the patient's normal anatomy can interfere with an accurate patient set up.

Another prospective series failed to support patient immobilization. In this study, patients treated in the supine position without immobilization actually had significantly less movement in the craniocaudal direction than patients treated in the prone position with immobilization (errors >5 mm: 24% compared to 11%. It is unclear whether differences in the patients' positions could explain this finding. In a prospective randomized study, it was demonstrated that the average simulation-to-treatment deviation of the isocenter position was 8.5 mm in a control group and 6.2 mm in an immobilized group. The use of immobilization devices reduced isocenter deviations exceeding 10 mm from 30.9% to 10.6% in the immobilized arm. The average deviations in the anteroposterior, right-left, and superior-inferior directions were reduced to 2.9 mm, 2.1 mm, and 3.9 mm for the immobilized group. In composite, the studies suggest that the haphazard use of immobilization devices may be worse than none at all. A well thought out and simple device that allows a comfortable and reproducible set up can reduce large errors. The commonly used immobilization devices are constructed of a melted plastic mold material, a solidified foam mold, or a reusable inflatable mold device.

Patient Positioning

Patients may be simulated and treated supine or prone. While some studies suggested that the prone position may result in less organ movement others have not confirmed this observation. In the prone position there may be greater rectal sparing, particularly in patients with large seminal vesicles. However, a larger percentage of the bladder may be included and associated with a slightly higher complication probability. There may also be more patient set up movement errors because some patients find the prone position less comfortable. Simulating and treating patients in a standardized set of conditions (e.g., bladder full) may reduce the variation in prostate position during the course of treatment. A prone position appears to be associated with greater prostate motion from normal breathing. The increased intra-abdominal pressure associated with breathing in a prone position results in significant movement of the prostate and seminal vesicles. One study evaluated the impact of breathing on the position of the prostate gland in four patients treated in four different positions in whom radiopaque markers were implanted in the periphery of the prostate using transrectal ultrasound (US) guidance prior to simulation. Fluoroscopy was performed in four different positions: prone in foam cast cradle, prone in thermoplastic mold, supine on a flat table, and supine with a false table under the buttocks. During normal breathing maximum movement of prostate markers seen in the prone position (cranial-caudal) ranged from 0.9 to 5.1 mm and anterior-posterior movement ranged up to 3.5 mm. In the supine position prostate movements during normal breathing was less than 1 mm in all directions. Deep breathing resulted in movements of 3.8 to 10.5 mm in the cranial-caudal direction in the prone position (with and without thermoplastic mold). This range was reduced to 2.7 mm in the supine position and to 0.5 to 2.1 mm with the use of a false tabletop. Deep breathing resulted in anterior-posterior skeletal movements of 2.7 to 13.1 mm in the prone position, whereas in the supine position these variations were negligible.

In a prospective randomized trial of the supine vs. prone position in patients undergoing conformal radiation therapy, 28 patients were randomized to commence radiation therapy in the prone or supine position and then change to the alternate position midway through their treatment course. After placement of fiducial markers in the prostate for daily prostate localization, the patients underwent computed tomography (CT) simulation and treatment planning in both positions. Observed prostate motion was significantly less in the supine position than the prone position. Pretreatment positioning corrections were required more often for patients in the prone position. A dose volume histogram analysis revealed more bladder wall, rectal wall, and small bowel in the high dose volumes when patients were in the prone position than in the supine position. Finally, patients were more comfortable in the supine position than the prone position. Seven patients that started in the supine position refused to be treated in the prone position due to discomfort. Other investigators have confirmed that prostate movement with respiration is significantly less with patients in a supine position. Regardless of the type of immobilization device used or the treatment position chosen, there is no replacement for a careful set up and clear instructions to patients to get into the same position every day.

Prostate Target Definition

The standard terms recommended in International Commission on Radiation Units and Measurements (ICRU) 50 for specifying dose prescription are summarized in the Table below.

Table. Definitions for Treatment Planning

Volume	General Definitions and Comments
GTV (gross tumor volume)	Tumor only, no margin. The entire prostate gland as determined by a CT scan commonly defines the GTV. Gross extension beyond the gland in a patient with a clinical stage T3, 4 cancers should be included as the GTV.
CTV (clinical target volume)	Includes margin around the GTV for regions of microscopic risk. This can include adjacent regions at risk of having subclinical disease such as the seminal vesicles or pelvic lymph nodes.
PTV (planning target volume)	Includes margin around the CTV to allow for patient movement, set up error, and organ movement.

Retrograde Urethrography

Variable recommendations for using retrograde urethrograms (RUGs) during treatment planning are found in the literature. RUG is primarily used for identifying the inferior border of the prostate. In the past the inferior border of the ischial tuberosities has been used as a landmark for defining the inferior field margin on conventional simulation radiograph films. Using the ischial tuberosities to define the lower border of the field will result in an inferior margin that is excessive in some patients and inadequate in others. RUG appears to more accurately define the inferior border of the prostate than conventional simulation plain films alone, because it takes into account large variations found in individuals who have either a high or low pelvic floor. However, because of variations in the functional length of the external sphincter, RUG is probably best

used to supplement computed tomography (CT) (see discussion below). The prostatic apex is 3 to 13 mm above the most proximal aspect of the urogenital diaphragm as defined by the urethrogram. Care should be taken not to over inflate the urethra with iodinated contrast as this may distend or move the prostate from its relaxed position. A carefully administered RUG does not significantly alter the position of the prostate gland.

CT-Based Prostate Localization

CT is the imaging approach of choice for treatment planning for external beam irradiation. CT simulators are readily available in most radiation oncology departments. Because of the rounded shape of the apical portion of the prostate, the most inferior portion of the gland often cannot be easily defined. Typically the location of the apex can be resolved to two or three CT slices obtained at 3 to 5 mm intervals. Because of difficulty visualizing the prostate on CT, a RUG can be used as a supplement to CT in this area. When RUG is obtained at the time of simulation it provides a landmark for comparing port films with simulation films to ensure that the apical portion of the gland is adequately covered. In the hands of a very experienced radiologist or radiation oncologist the use of CT may be adequate. The radiation oncologist should use multiplanar reconstructions to facilitate prostate definition on a treatment planning CT. Both sagittal and coronal views through the gland can help avoid contouring tissue beyond the limits of the gland both at the apex and the base.

MRI-Based Prostate Localization

Magnetic resonance imaging (MRI) may be more accurate in delineating the prostate and seminal vesicles than CT. CT overestimates the size of the gland approximately 27% to 32%. Several publications have shown some discrepancy (0.5 to 1 cm) in defining the location of the apex of the prostate using CT or MRI scanning. One study evaluated co-registration of CT and MR images in the radiation treatment planning of six patients with localized prostate cancer to assist with GTV delineation and identification of prostate position during radiation therapy. The overall magnitude of contoured GTV was similar for MR and CT; however, there were spatial discrepancies in contouring between the two modalities. The greatest systematic discrepancy was at the posterior apical prostate border, which was 3.6 mm more posterior on MRI than on CT-defined contouring. Another study compared CT, MRI, and urethrography to define the prostate apex. They concluded that MRI is superior to CT or urethrography for localizing the prostatic apex. They suggested that MRI be used for all patients undergoing radiotherapy for prostate cancer to define the apex.

Endorectal MRI may detect extracapsular tumor extension, seminal vesicle invasion, or neurovascular bundle involvement with greater sensitivity, specificity and accuracy than clinical findings alone. In a series of 38 patients undergoing preoperative endorectal MRI imaging, the accuracy rates in detecting capsular penetration, seminal vesicle invasion, and neurovascular bundle involvement were 84%, 97%, and 97%, respectively. In a larger series of 344 patients, it was reported that endorectal MRI scanning improved the prediction of extracapsular extension over a predictive model that included only clinical variables of PSA, Gleason score, clinical stage, volume of cancer in the biopsy specimens and

perineural invasion. Endorectal MRI appears particularly helpful in patients who have intermediate or high-risk clinical features.

Magnetic resonance spectroscopy (MRS) can detect variable concentrations of citrate, choline and creatine in prostate tissue and improve the accuracy of detecting and localizing prostate cancer.

MRI may also allow better identification of structures adjacent to the prostate that are associated with erectile function. One study described 25 patients with localized prostate cancer who underwent both CT and MRI-based treatment planning. They were able to spare the critical erectile structures more often with an MR T2 and MRI angiogram based treatment plan than with a plan using conventional CT-based contouring. At this time, it is unclear whether sparing of the erectile tissues with MRI-based radiation treatment planning will lead to better sexual outcome or quality of life. It also remains to be proven that sparing of these tissues will not compromise long-term tumor control.

The disadvantages to MRI-based prostate localization are limited availability, CT-MR fusion uncertainties, treatment planning warping, and a loss of radiography density information for radiation dose calculation and digital reconstructed radiograph creation for treatment verification. Several centers are exploring methods to reduce the dosimetric and positional uncertainties associated with MR simulation. At this time it is reasonable to use MRI to facilitate the definition of target volumes, especially if CT-MR fusion capabilities or an MRI simulator are available.

Defining the Gross Tumor and the Clinical Target Volume

Because prostate cancer is often found to be multifocal at the time of radical prostatectomy, the entire gland is commonly considered the gross tumor volume for radiation treatment planning purposes. The CTV may expand the gross tumor volume to account for direct extension, or the CTV can be extended to encompass adjacent organs or regions of spread. In prostate cancer, the CTV may encompass the seminal vesicles and possibly the regional pelvic lymph nodes.

Additional margin for possible extraprostatic extension (EPE) has been recommended by several authors. In a study of radical prostatectomy specimens, it was demonstrated that EPE was present in 28% of 376 patients. When EPE was present, the average radial distance of cancer from the prostate capsule was 0.8 mm with a range of 0.04 to 4.4 mm. The decision to add additional CTV margin may be most important in patients with high-risk features, such as a PSA over 20, Gleason score more than 7, or bulky tumors (T2c or greater).

In selected patients it is necessary to include the seminal vesicles in the CTV, which in most patients are well demonstrated on the cross section CT scans of the pelvis. Nomograms may be used to determine the probability of extraprostatic extension, seminal vesicle, or pelvic lymph node involvement using clinical stage, pretreatment PSA, and Gleason score. One study published an analysis of 344 radical prostatectomy specimens in which the length of seminal vesicles, length of involvement by carcinoma, and percentage of seminal vesicle involved were measured. They found an excellent correlation between the various prognostic parameters and the probability of seminal vesicle involvement. Also, in 81

patients with positive seminal vesicle involvement, the median length of tumor presence was 1 cm. In the entire population, 7% of patients had seminal vesicle involvement beyond 1 cm. They concluded that in selected patients seminal vesicles should be treated and only 2.5 cm (approximately 60% of the seminal vesicle) should be included within the CTV, unless there is radiographic evidence of involvement.

In cases where the disease is confined to the gland (clinical stages T1-2) but the risk of seminal vesicle invasion exceeds 15%, 2 CTVs can be defined. The first encompasses the prostate and the seminal vesicles and the second boost CTV is the prostate alone. In these cases, a radiation dose that controls subclinical disease is prescribed to the first target volume, and a higher dose is intended for the prostate itself. When there is evidence of EPE on physical examination or imaging modalities such as MRI (clinical stage T3), the seminal vesicles should be included for the total radiation dose prescription.

Planning Target Volume definition

The magnitude of the PTV margin depends on several factors. Treatment setup errors can vary by the method of patient positioning and immobilization. Internal organs, including the prostate gland, can shift because of variable filling of the rectum and bladder. The shifts can be asymmetric, with most movement occurring in the anterior and posterior directions. In order to assure that an adequate radiation dose treats the CTV, an appropriate PTV margin must be added. There is a tradeoff between assuring nearly 100% coverage during each treatment and the volume of adjacent organs irradiated unnecessarily.

One study evaluated 17 patients with prostate cancer who underwent CT scanning for treatment planning and three subsequent CT scans obtained at approximately 2-week intervals during external beam fractionated irradiation. The authors observed CTV motion of 0.9 mm (left to right), 3.6 mm (cranial-caudal), and 4.1 mm (anterior-posterior) directions. From this study, the authors concluded that margins between the CTV and PTV necessary to enclose 95% of the PTV were 7 mm in the lateral and cranial-caudal directions and 11 mm in the anterior-posterior (AP) direction.

Another study evaluated prostate and seminal vesicle motion in 50 patients treated in the prone position using CT scans for initial treatment planning and three scans obtained throughout the course of radiation therapy. Before the initial CT scans, patients had an enema and were given 250 ml of bowel contrast by mouth. Patients had an empty bladder, and 10 cc of air was inserted into the rectum via rectal catheter. Prior to all CT scans, patients voided, and no additional procedures were performed. Relative to the initial planning CT, mean displacements of the prostate were -1.2 ± 2.9 mm in the AP, -0.5 ± 3.3 mm in the superior/inferior, and -0.6 ± 0.8 mm in the lateral direction. The seminal vesicle displacements were -1.4 ± 4.9 mm, 1.3 ± 5.5 mm, and - 0.8 ± 3.1 mm in the AP, superior-inferior (SI), and lateral directions, respectively (negative values indicated displacements to the posterior, inferior, and left directions). A combination of rectal volume larger than 60 cc or a bladder volume larger than 40 cc was found to be predictive for systematic deviations of the prostate and seminal vesicles of more than 3 mm. Based on the data and the intent to have the prescription dose achieve at least 93% coverage of the CTV, the authors

calculated the margins to be added to the CTV for defining the PTV. Based on these reports, it is apparent that beyond the CTV, additional margins of 5 to 8 mm are necessary to provide adequate coverage of the prostate and 6 to 11 mm for adequate coverage of the seminal vesicles when there is no organ distension that would result in a systematic error.

Localization for Prostate Radiation Therapy

Megavoltage imaging with position correction can reduce the magnitude of systematic setup errors in daily external beam radiation therapy. One study demonstrated in a randomized trial that an integrated megavoltage imaging system with repositioning during treatment would improve the accuracy of treatment from 4.3 mm to 2 mm and reduce the frequency of displacement errors >5 mm from 69% to 7%. Another study reported a time trend in patient setup deviations on the order of 4 to 11 mm. They argued that portal images should be taken during the entire course of treatment and that verification imaging should not be limited to the start of therapy.

New strategies to reduce the uncertainty in daily treatment delivery and the magnitude of the PTV margin have been introduced. These methods employ daily imaging of the prostate in the treatment room. Radiopaque implanted fiducial markers can be imaged with electronic portal imaging or stereoscopic kilo voltage imaging devices. One study evaluated prostate motion in 55 patients in whom gold seeds were implanted at the base of the gland. Initial simulation was obtained in a supine position with a full bladder and repeated after patients received 40 Gy. Prostate motion was observed in the posterior direction (5.6 mm ± 4.1 mm) and in the inferior direction (5.9 mm ± 4.5 mm). In 30% of the patients the base of the prostate was displaced posteriorly and in 11% in the inferior direction by more than 10 mm. A series of 10 patients reported that margins could be reduced using daily fiducial marker localization and pretreatment position correction. After prostate localization and adjustment, the position errors were reduced to 1.3 to 3.5 mm left-right, 1.7 to 4.2 mm anterior-posterior, and 1.6 to 4.0 mm inferior-superior in prone patients, and 1.2 to 1.8 mm left-right, 0.9 to 1.8 mm anterior-posterior, and 0.8 to 1.5 mm inferior-superior in supine patients. New radiofrequency transponders can localize the prostate in a manner similar to gold markers but without additional radiation dose to the patient. These transponders can also be tracked real-time during a treatment session, allowing for immediate intervention if the prostate moves outside the radiation field.

Transabdominal Ultrasound

Transabdominal ultrasound (US) has been used to localize the prostate for treatment planning and during daily radiation therapy delivery with accuracy parallel to that of CT scanning of the pelvis. One study evaluated 23 patients with CT simulations on whom prostate-only fields based on CT scans were created with no PTV margin. Ten of the patients also had prostate localization with a transabdominal ultrasound system. The absolute magnitude differences in CT and US were small (AP mean 3 mm ± 1.8 mm, lateral mean 2.4 mm ± 1.8 mm, superior/inferior mean 4.6 mm ± 2.8 mm). In a second study, they evaluated 35 patients that had US localization in the CT simulation room. There was a high correlation between the CT-defined position of the prostate and the position

determined by US. The authors felt the transabdominal US was simple and expeditious and improved their ability to localize the position of the prostate with the patient at the treatment machine for daily irradiation. Using an US-based system, another study reported that without US localization, organ motion would have caused the CTV to move outside the PTV margin in 23.3% to 41.8% of the treatments.

CT Imaging

Newer linear accelerators and treatment rooms have introduced tomographic volumetric imaging capabilities that allow daily capture of 3D image data. Both megavoltage and kilo voltage CT reconstructions can display the daily position of the prostate and adjacent organs at risk, thereby allowing treatment position to be adjusted to assure the entirety of the target is in the daily treatment volume.

Endorectal Balloon

Use of an endorectal balloon during daily treatment potentially stabilizes the position of the gland. The balloon also moves the prostate anteriorly, allowing shielding of the posterior rectal wall. An endorectal balloon is a controlled intervention that can be reproduced during the course of radiation therapy. Air in the balloon may decrease the rectal surface dose by decreasing the electronic buildup and equilibrium at the air-soft tissue interface. One study reported results of 100 consecutive patients treated with intensity modulated radiation therapy (IMRT) and an endorectal balloon. Ten of those patients also participated in a prostate motion study following gold seed implantation. Each of these ten patients underwent 10 CT scans during the course of their radiation therapy. The mean and standard deviation of superior-inferior target displacements were 0.92 mm and 1.78 mm, respectively. Of the 100 patients treated with a rectal balloon, 80% had no rectal complaints and 11% and 6% had grade 1 or 2 acute toxicity, respectively. They measured the radiation dose at a balloon-tissue interface using a phantom. The dose at the air-tissue interface is approximately 15% lower than the dose at the same point without an air cavity. The dose builds up rapidly so that at 1 and 2 mm away from the interface, the dose is only approximately 8% and 5% lower, respectively.

Conventional and Conformal Blocking (2-D, 3-D and IMRT)

Standard blocking or conventional treatment planning techniques have traditionally been based on the use of bony landmarks or CT images to estimate the approximate location of the prostate. Standard blocking techniques usually involve the use of open square or rectangular blocks to deliver radiation by bilateral arcs or rectangular fields with minimal blocking.

3-D conformal radiotherapy (3-DCRT) may allow higher doses to be delivered than conventional radiation therapy because of greater flexibility in beam arrangements.

Several prospective trials have demonstrated that 3-DCRT can allow safe escalation of radiation dose with either equal or lower rates of morbidity compared to historical or contemporary controls. The RTOG® prospective dose escalation trial reported the administration of minimum PTV doses from 64.8 Gy to 79.2 Gy

in 1.8 Gy/day fractions and 74 Gy to 78 Gy in 2 Gy/day fractions with lower than expected incidence of grade 3 or worse intestinal or urinary toxicity based upon comparisons to historical controls. In a British randomized trial at the Royal Marsden Hospital and NHS Trust, a reduction in grade 1 and 2 late radiation proctitis was reported in men receiving 3-DCRT compared to men treated with conventional radiation techniques to doses of 60 to 64 Gy. In a French cooperative group randomized trial, there was no increase in acute side effects in patients treated to 70 Gy compared to 80 Gy with 3-DCRT.

IMRT has recently emerged as the "next generation" of available treatment planning technology. IMRT planning begins in nearly an identical manner to that of forward planned 3-DCRT; however, patient positioning and reproducibility is far more critical due to the sharp dose gradients that can be seen with this modality. Daily target localization method is critical in patients receiving IMRT for prostate cancer. Suitable methods include transabdominal US, intraprostatic fiducial markers with daily megavoltage portal or radiographic imaging, endorectal balloon immobilization, or daily in-room CT imaging. IMRT treatment planning requires defining dose constraints for the target and each critical structure. IMRT creates more heterogeneity of dose than 3-DCRT, and the planning prescription needs to define a minimum dose to cover a predetermined volume of the PTV as well as a maximum dose to a small volume inside the PTV. Dose limits to organs at risk need to take into account both upper dose limits as well as the volume of those organs that are allowed to exceed those limits.

Dose Prescription for Localized Prostate Cancer

Several institutions have reported a radiation dose response for localized prostate cancer based on retrospective reviews. In some reports, there has not been a benefit for dose escalation above 70 Gy for low-risk prostate cancer. One study reported no benefit to doses greater than 77 Gy compared to 67 to 77 Gy for low-risk patients. The Fox Chase Cancer Center experience did not show a dose response for doses higher than 72 Gy. This lack of benefit to higher doses may be due to the small local tumor burden that is readily controlled with conventional doses. On the other hand, investigators from the Cleveland Clinic and Memorial Sloan Kettering have shown a biochemical disease free survival benefit for patients with low risk disease who receive escalated doses with 3-DCRT or IMRT.

Intermediate risk disease benefits from escalated radiation doses in most retrospective analyses. One study reported 5-year biochemical disease free survival rates of 24%, 65%, and 79% for patients receiving isocenter doses of <72 Gy, 72-75.9 Gy, and ≥76 Gy, respectively. Another study reported 5-year biochemical disease free survival rates of 27%, 51% and 83% for radiation doses of ≤68 Gy, 68-72 Gy, and >72 Gy, respectively.

Patients with high-risk disease do not uniformly demonstrate a benefit to escalated radiation doses. This may be due to the greater burden of subclinical metastases in patients with high presenting PSA or high grade disease. A study from the Cleveland Clinic reported improved 5- year biochemical disease free survival rates for high risk patients of 21%, 29%, and 71% for radiation doses of ≤68 Gy, 68-72 Gy, and >72 Gy, respectively. Another study suggested a dose response for biochemical disease free survival for high risk patients. The authors suggested that a 5 Gy dose increase beyond 78 Gy may improve PSA control for

these patients. Several randomized trials have been undertaken to demonstrate whether there is a benefit to high dose 3-DCRT. The first completed and published study demonstrated a significant biochemical disease free survival in patients randomized to receive 78 Gy compared to 70 Gy. In this trial all patients began with radiation to a limited pelvic field with a standard 4 field arrangement. Patients were then randomized to receive a conventional field boost to a total isocenter dose of 70 Gy or a 3-DCRT boost to a total isocenter dose of 78 Gy. The largest gain from this 8 Gy dose increase was seen in the patients with pretreatment PSA >10 ng/mL. In those intermediate risk patients the 5-year biochemical disease free survival rates were 72% and 44% for 78 G or 70 Gy, respectively. Another study demonstrated an advantage to high dose radiation therapy in both low-risk and high-risk patients.

Normal tissue tolerance plays an important role in 3-DCRT and is critical in IMRT treatment planning. Investigators from MD Anderson Cancer Center conducted a prospective trial randomizing patients to 70 Gy or 78 Gy using conventional or 3-D conformal approaches. There was no difference in acute toxicity despite the use of higher doses. However, with longer follow-up there was a reduction in late complications with the use of 3-D conformal technique despite the use of higher doses. Based on their review of rectal toxicity in patients who received 3-DCRT, the Memorial Sloan Kettering dose escalation study recommended keeping ≤60% of the rectal wall to receive 40 Gy and ≤30% of the rectal wall should receive ≥75.6 Gy to minimize the risk of grade 2 or greater rectal toxicity.

Investigators at MD Anderson reported that the organ at risk volumes receiving high radiation doses are of major importance. The incidence of grade II/III toxicity at 3 years decreased from 28% to 12% if less than 25% of rectum volume was 70 Gy or more.

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate external beam radiation therapy for patients with clinically localized prostate cancer

POTENTIAL HARMS

Radiation therapy is associated with toxicity such as proctitis, intestinal toxicity, urinary toxicity, severe rectal bleeding.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Michalski JM, Roach M III, Merrick G, Anscher MS, Beyer DC, Lawton CA, Lee WR, Pollack A, Rosenthal SA, Vijayakumar S, Carroll PR, Expert Panel on Radiation Oncology-Prostate. External beam radiation therapy treatment planning for clinically localized prostate cancer. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 12 p. [111 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2006)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology–Prostate

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Jeff M. Michalski, MD, MBA; Mack Roach III, MD; Gregory Merrick, MD; Mitchell S. Anscher, MD; David C. Beyer, MD; Colleen A. Lawton, MD; W. Robert Lee, MD; Alan Pollack, MD, PhD; Seth A. Rosenthal, MD; Srinivasan Vijayakumar, MD; Peter R. Carroll, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Roach M, Blasko JC, Perez CA, Beyer DC, Forman JD, Hussey DH, Lee WR, Paryani SB, Pollack A, Potters L, Scardino P,

Schellhammer P, Leibel S. Treatment planning for clinically localized prostate cancer. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun;215(Suppl):1441-8.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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